REMARKS

Status of the Claims

Claims 26, 31, 37, and 38 have been amended. Claims 27-30 and 33 have been canceled without prejudice. Claims 26, 31, and 35-39 are in the case.

Objection to Claims

The objection to Claims 27-29 as improperly dependent claims is moot.

Applicant submits that the claims 27-29 were in proper dependent form. As claims 27-29 are now canceled, however, the objection is moot.

Rejection of Claims Under 35 USC §112

Claims 26 and 31 are fully enabled by the Specification.

The Action rejects claims 26-29, 31, and 33 as being enabled only for treatment of metastatic disease. As claims 27-29 and 33 are now canceled, however, the rejection to those claims is moot. Applicant traverses because in addition to the treatment of metastatic disease, the Specification is enabling for treatment of neoplastic disease including pre malignant disease, tumors and tumors that are premetastatic or predisposed to become metastatic. It is well known that prostate disease is a progression from benign hyperplasia to tumor to metastasis and the level of caveolin expression rises as the tissues progress toward metastasis.

As stated in the Specification:

> [0008] As determined from the epidemiological and clinical studies, most cancers develop in slow stages from mildly benign into malignant neoplasms. Malignant cancer usually begins as a benign localized cell population with abnormal growth characteristics called dysplasia. The abnormal cells acquire abnormal growth characteristics resulting in a neoplasia characterized as a cell population of localized growth and swelling. If untreated, the neoplasia in situ may progress into a malignant neoplasia. Several years, or tens of years may elapse from the first

sign of dysplasia to the onset of full blown malignant cancer. This characteristic process is observed in a number of cancers. Prostate cancer provides one of the more clear examples of the progression of normal tissue to benign neoplasm to malignant neoplasm.

The Specification states in [0017] that caveolin expression increases in metastatic human prostate cells as compared to primary tumors and agents, and blocking the activity of caveolin in metastatic cells **or cells predisposed to metastasis** would be useful in treatment of human prostate tumors. A comparison of primary and metastatic tissues is shown in Table 1, Example 1 of the Specification. Furthermore, the Specification at [0080] incorporates Yang et al., submitted to the Examiner as Ref. HHH in an Information Disclosure Statement on October 22, 2003, and attached as Exhibit 4. The Yang reference was published by the inventor after the priority date of the present application and shows the increased expression of caveolin in metastatic prostate cells relative to cells from primary tumors, Fig. 1C.

The Specification thus establishes association of increased caveolin expression from normal to primary tumor to metastatic neoplastic disease in the human prostate. The data in Table 1, and in the Yang paper also establish that the caveolin is also present in pre-metastatic or primary tumors. Therefore, the claimed methods are not limited to treatment of metastatic tissue, but also include treatment of primary tumors as well as pre-malignant neoplasia.

The claims are thus fully enabled for treatment of primary and metastatic prostate cancer as well as those cells that are predisposed to becoming malignant or metastatic. Applicant respectfully requests that the rejection under §112 be withdrawn.

Rejections Under 35 USC §103

A. The Action rejects 26, 30, 31,and 33 as obvious over Yang et al. *Clinical Cancer*

Research vol. 4, 1873-1880, published August, 1998, in view of Meredith et al. (Prostate Carcinoma Radioimmunotherapy, vol 35, col 1017-1022, 1994). As claims 30 and 33 are now canceled, however, the rejection to those claims is moot. Applicant traverses the Action's application of Yang as prior art to the present claims for at least the reasons stated below.

The Yang reference is not available as prior art to the claims, because (i) the description in Yang does not go beyond what Applicant had previously filed in Provisional Application No. 60/064351 and (ii) Yang is the inventor's own work.

The Action relies on Yang for the teaching that caveolin is overexpressed in metastatic prostate tissue, referring to figures 1 and 2 of Yang. The provisional application, No. 60/064351, to which the present application claims benefit of priority also discloses an increased expression of caveolin in metastatic lymph nodes on page 25, Table 3. In addition, the provisional application states that immunohistology of tissue sections reveals both elevated levels and distinct distribution of caveolin protein in metastatic human prostate when compared to primary human prostate tumor, as shown in Fig. 11 of the provisional application.

The Yang paper, therefore, cannot be prior art because it merely describes what was already enabled in the provisional application prior to its publication.

Yang is not available as prior art under 102(a) because Yang is the inventor's own work.

For Yang to be applied against the present claims, it must be available under 35 USC §102(a) since it was published less than a year prior to the filing date of the present application, the priority date currently recognized by the Examiner. However, Yang cannot be prior art under §102(a) because it is the inventor's own work.

The Yang paper lists ten co-authors in addition to the inventor, Dr. Timothy C. Thompson. The co-authors of the Yang paper worked under the direct supervision and control of Dr. Thompson as related to this invention.

As stated in MPEP §715.01(c)I:

> Where the applicant is one of the co-authors of a publication cited against his or her application, he or she may overcome the rejection by filing an affidavit or declaration under 37 CFR 1.131. Alternatively, the applicant may overcome the rejection by filing a specific affidavit or declaration under 37 CFR 1.132 establishing that the article is describing applicant's own work. An affidavit or declaration by applicant alone indicating that applicant is the sole inventor and that the others were merely working under his or her direction is sufficient to remove the publication as a reference under 35 U.S.C. 102(a). *In re Katz*, 687 F.2d 450, 215 USPQ 14 (CCPA 1982).

Attached hereto is a declaration of Dr. Thompson stating the roles of the co-authors of the Yang paper and establishing that none of the co-authors contributed to the conception of the claimed inventions.

The Action also relies on Meredith in making the obviousness rejection, based on the description of an antibody that recognizes the tumor antigen, TAG-72. Nothing in Meredith, however, suggests that such antibody has any relation to the caveolin protein, nor that the caveolin protein is associated with the progression of a benign neoplasia to malignany and then the metastatic spread of prostate cancer.

Thus the Meredith reference alone cannot render any of the claims obvious, which it would have to in order to maintain this rejection since the Yang reference is not prior art. Applicant requests therefore that the rejection of claims 26 and 31 as obvious over Yang in view of Meredith be withdrawn.

B. The Action also rejects Claims 26, 30-31, 33 and 35-39 as obvious over

Goethuys, et al. or Nasu et al., in view of Yang and Meredith. As claims 30 and 33 are now canceled, however, the rejection to those claims is moot.

Claims 26, 31, and 35-39, as drawn to a combination of anti-caveolin and androgen ablation are not obvious over the cited art, as neither Yang nor Nasu are available as prior art, and the combination of Meredith and Goethuys does not teach or suggest all limitations of any of the claims.

Of the cited references, Yang is not available as prior art as discussed above. In addition, Nasu is not available as prior art because this paper was published less than a year prior to the filing date of the present application, and the Nasu reference is also the inventor's own work.

Nasu is also not available as prior art as it is only available under 102(a) and is the inventor's own work.

The Nasu paper lists nine co-authors in addition to the inventor, Dr. Timothy C. Thompson. The co-authors of the Nasu paper worked under the direct supervision and control of Dr. Thompson as related to this invention.

In the attached declaration of Dr. Thompson, the roles of the co-authors of the Nasu paper are discussed. The declaration establishes that none of the co-authors of the Nasu paper contributed to the conception of the claimed inventions.

The combination of Goethuys and Meredith does not establish a prima facie case of obviousness.

Although Goethuys is said in the Action to teach the association of androgen and prostate cancer, and also to describe androgen ablation in combination with immunotherapy, Applicant finds no description in Goethuys of the association of caveolin with metastasis or with androgen sensitivity, and furthermore, no suggestion of

restoring androgen sensitivity by treatment with an anti-caveolin agent. Additionally, none of these elements of the claims that are missing from Goethuys are described in Meredith.

Therefore the combination of Goethuys with Meredith would not teach or suggest the claimed invention since the combination neither teaches nor suggests the use of an anti-caveolin antibody in the inhibition of metastasis, nor in restoring androgen sensitivity.

The cited references, therefore, do not establish the obviousness of any of the rejected claims. Applicant respectfully requests, therefore that all rejections under §103 be withdrawn.

Conclusion

Applicant submits that all of the Examiner's rejections and objections are overcome in light of the preceding amendment, arguments and evidence, and requests that all rejections be withdrawn and the pending claims be allowed without further amendment or prosecution.

If the Examiner has any questions or suggestions that might expedite allowance of the claims, a telephone call to the undersigned representative would be welcomed.

Respectfully submitted,

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